Remarks

Claims 10, 11, 18, 30, and 31 are under examination, claims 1-9, 12-14, and 19-29 having been previously cancelled and claims 15-17 having been withdrawn as claiming non-elected subject matter.

Claims 10, 11, 18, and 30 have been amended herein. These claims have been amended to more clearly state that which applicants believe to be their invention.

Claim 32 has been added herein.

Applicants note that the Examiner admits that SEQ ID NO:9 is free of prior art.

Claim 11 has been amended for clarification purposes by amending the phrase "polypeptide comprises an amino acid of SEQ ID NO: 9" to recite "polypeptide comprises an amino acid sequence of SEQ ID NO: 9". The word "sequence" was merely added to more clearly state that which Applicants believe to be their invention. Furthermore, this amendment merely places the language in conformity with the other claims.

Claim 10 has been amended by amending the phrase "purified or recombinant polypeptide" by deleting the term "or recombinant" such that it now recites "purified polypeptide", and by adding the descriptor "bioactive" for the variants of SEQ ID NO:9. These amendments are supported by the specification as filed and are discussed more fully below.

Claim 18 has been amended to depend from claim 10. It has also been amended by deleting the term "SAMP32 polypeptide", as it now depends for the SEQ ID NO:9 peptides of claim 10. Claim 18 has been further amended to recite "bioactive polypeptide" instead of "polypeptide". These amendments are supported by the specification as filed and are discussed more fully below.

Claim 30 has been amended to recite "bioactive fragment" of SEQ ID NO:9, instead of just "fragment" of SEQ ID NO:9. This amendment is supported by the specification as filed and is discussed more fully below.

Claim 32 has been added. As mentioned above, claim 10 was amended by amending the phrase "purified or recombinant polypeptide" by deleting the term "or recombinant" such that it now recites "purified polypeptide". To that end, claim 32 was added to incorporate the term "recombinant" because it was deleted from claim 10. This amendment is supported by

the specification as filed, including prior claim 10, and is discussed more fully below.

Response to rejection under 35 U.S.C. § 112, first paragraph, written description-

Claims 10, 18, and 30 stand rejected under 35 USC § 112, first paragraph as containing subject matter that was not adequately described in the specification.

It is the opinion of the Examiner that claim 10 lacks adequate written description because it recites, inter alia, amino acid sequences that differ from SEQ ID NO:9 by a single mutation, wherein the single mutation represents a single amino acid deletion, insertion, or substitution, asserting at page 3 that "the structure of the amino acid with its mutation(s) is not provided". The Examiner further asserts that the structure of the polypeptide does not correlate with its function. The Examiner also asserts that it is not clear whether the polypeptide is purified or recombinant, because the word "or" is used in the claim.

Although not necessarily agreeing with the reasoning of the Examiner, and to expedite prosecution of the application, claim 10 has been amended regarding the term "or" by amending the phrase "purified or recombinant" to recite merely "purified". New claim 32 has been added which recites the same elements as claim 10, except that the term "recombinant" is used, instead of the term "purified" as recited in amended claim 10. This amendment is supported by previous claim 10 and throughout the specification as filed.

Applicants traverse the Examiner's rejection as to the use of the term mutation as recited in claim 10, asserting that its use is adequately described in the specification as filed and that the structure of the polypeptide does correlate with its function. However, in order to expedite prosecution of the application, Applicants have also amended claim 10 by adding the term "bioactive" with regard to the elements reciting amino acid substitutions or mutations. The reasons that Applicants assert that the use of mutations of SEQ ID NO:9 are adequately described and that the structure and function of the peptides are correlate are provided below.

In *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996), the Court of Appeals for the Federal Circuit pointed out that literal support is not required in order to satisfy the written description requirement:

> If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed

> invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. For example, in *Ralston Purina Co. v. Far-Mor-Co., Inc.*, 227 USPQ 177, 180 (Fed. Cir. 1985), the trial court admitted expert testimony about known industry standards regarding temperature and pressure in "the art of both farinaceous and proteinaceous vegetable materials." The effect of the testimony was to expand the breadth of the actual written description since it was apparent that the inventor possessed such knowledge of industry standards of temperature and pressure at the time the original application was filed.

Therefore, it is clear that the invention need not be described in *ipsis verbis*, *i.e.*, literally, for purposes of the written description requirement under 35 U.S.C. §112, first paragraph. Rather, what is needed is that the skilled artisan understand, based upon the disclosure in the specification as filed, and the knowledge imputed to the skilled artisan at the time the specification was filed, that the inventor had possession of the claimed subject matter.

Furthermore, the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office has recently weighed in regarding enablement and written description requirement for sequences. Ex parte Bandman, No. 2004-2319 (BPAI 2005). At page 3 the Board stated that "[t]he written description requirement of 35 U.S.C. § 112, first paragraph, does not require a description of the complete structure of every species within a chemical genus (citing Utter v. Hiraga, 845 F.2d 993, 998, 6 USPQ2 1709, 1714, Fed. Cir. 1988). The Board further discussed what types of properties might be relevant to variants of a sequence, and the requirement that an Examiner must adequately explain and/or provide evidence to support a rejection asserting lack of correlation between structure and function (Id., page 5)

Applicants respectfully submit that the skilled artisan would have understood, based upon the disclosure provided in the specification as filed, and knowledge available at the time the application was filed, that the inventors had possession of the present invention as claimed in **amended** claim 10 and new claim 32. For example, amended claim 10, as well as amended claim 30 and new claim 32, now recite "bioactive" sequences. As defined in the specification a bioactive fragment of SAMP32/SEQ ID NO:9 encompasses natural or

synthetic portions of the polypeptide that is capable of specific binding to at least one of the natural ligands of the native polypeptide (page 6, lines 1-4). This definition comports with the Boards finding in Ex parte Bandman. Accordingly, based on the definition provided in the specification, applicants have specified a distinguishing attribute of the members of the claimed genus - they all must bind to a ligand that binds to the original sequence.

Applicants are not attempting to generically claim all "variants" of SEQ ID NO:9, but rather they are merely claiming minor altered forms of SEQ ID NO:9 that have the requisite functionality. One of ordinary skill in the art would recognize that the description of the claimed invention is complete in light of the amino acids sequence provided, coupled with the functional characteristics of the claimed genus and the limitations placed on the members of the genus. Rather than providing a specification that includes an exhaustive "laundry list" of all possible amino acid fragments or mutations of SEQ ID NO:9 that meet the criteria of the claims, applicants have selected a formula to describe the claimed compounds that meet the criteria of the present invention. One of ordinary skill in the art would readily appreciate that altering a single arbitrary amino acid of SEQ ID NO:9 would be unlikely to make the present protein non-functional, particularly when that alteration is a conservative amino acid substitution or mutation (see page 7, line 24 to page 8, line 2; page 5, lines 9-20). Applicants are simply attempting to claim a scope of protection reasonably commensurate with their discovery of a protein (SEQ ID NO:9) that has utility in contraceptive applications. Applicants have narrowly tailored their claims to include only those derivatives of the originally discovered protein (SEQ ID NO:9) that one of ordinary skill in the art would accept were in the possession of the applicants, based on the specification.

Furthermore, applicants have specified the function the particular claimed fragments are to possess, they must bind a ligand that binds to SEQ ID NO:9. One of ordinary skill in the art readily appreciates the procedures to analyze whether a particular fragment and/or substitution or mutation meets the claim criteria. For example, antibody binding assays are well known to those skilled in the art and would require no undue experimentation to analyze whether a particular fragment has the requisite activity. Applicants have not disclosed the exact location of the modifications claimed, however applications respectfully submit that the written description does not require such detail when functional characteristics are coupled

with structure as is in the current claims. For example, it is clear that a written description for an ability to bind does not require the description of the specific amino acid sequence to which the ligand binds. Only the overall protein needs to be identified, coupled to the function that the fragment or homolog has the same function/activity as the parent protein or sequence. Similarly, Applicants respectfully submit they are not required to identify the exact sequence of each any every fragment of the SEQ ID NO:9 that is a bioactive fragment (i.e., remains capable of binding to an antibody or ligand that specifically binds to SEQ ID NO:9). Applicants have provided the overall structure of the invention (a 294 amino acid sequence) coupled with functional characteristics (i.e., it must bind to a ligand of the original protein) that define the members of the claimed genus. Furthermore, applicants note that these functional limitations of the claimed invention were part of the original specification and claims and constitute the invention as originally claimed and in possession of the inventors at the time the application was filed.

Applicants respectfully submit that in accordance with the USPTO's written description guidelines, applicants have provided:

1) Specific structure as represented by the amino acid sequence of SEQ ID NO:9. This sequence defines and limits the structure of the claimed bioactive fragments; and

2) functional characteristics of the genus, by stating the bioactive fragments will bind to the ligands of the native polypeptide, including antibodies raised against the native polypeptide. One of ordinary skill in the art would readily appreciate how to screen for the bioactive fragments that are claimed. Applicants respectfully submit that the specification provides sufficient structure and functional characteristics to meet the written description requirements of 35 U.S.C. § 112, second paragraph.

Claim 10 is further directed to specific variants of SEQ ID NO:9 wherein the sequence differs only by one or more conservative amino acid substitutions. Applicants respectfully submit that they are entitled to claim their invention beyond the specific examples provided in the specification. Otherwise, one of ordinary skill in the art could readily avoid the claims by making minor and non-substantive changes to the invention while enjoying the benefits of the inventors' invention. Accordingly, one embodiment of the

present invention is directed to minor derivatives of disclosed SEQ ID NO:9. (see Ex parte Bandman, No. 2004-2319 (BPAI 2005)).

Those skilled in the art are well aware that amino acids can be grouped into various classes based on their physical properties. Substituting one amino acid for another amino acid within the same group (i.e. a conservative amino acid substitution) typically does not affect the underlying properties of the protein. Applicants have described at page 5, lines 8-20 the specific groups of amino acids that constitute the conservative amino acid groups. Furthermore, applicants have specified in claims the number of conservative amino acid substitutions that are encompassed by the claimed invention. Applicants have not specified a specific location for these substitutions, because based on the vary nature of a conservative amino acid substitution it should not matter where the substitution is made. Furthermore, as stated above one of ordinary skill can readily ascertain if the alteration has modified the activity of the protein.

Applicants respectfully submit that they have provided a description of structure for the genus (i.e., SEQ ID NO:9) and provided specific limitations on the class of compounds claimed (only those that are identical to SEQ ID NO:9, but for the inclusion of up to 10-20 amino acid substitutions) sufficient to meet the written description requirement of 35 U.S.C. § 112, second paragraph. Applicants respectfully request the withdrawal of the rejection of claim 10 under 35 U.S.C. § 112, second paragraph.

In the view of the Examiner, claim 18, which recites an antigenic composition comprising a SAMP32 polypeptide, lacks adequate written description. It is asserted by the Examiner that there is no structure or function that corresponds to the SAMP32 polypeptide. Although not necessarily agreeing with the reasoning of the Examiner, claim 18 has been amended from being an independent claim to depending from claim 10. That is, the term "SAMP32 polypeptide" is deleted, and instead the claim recites in dependent form a "polypeptide of claim 10". As discussed above, claim 10 now recites "bioactive" peptides. This amendment is supported at page 5, lines 28-29, where the term "SAMP32 polypeptide" is defined as "the term "SAMP32 polypeptide" and like terms refers to polypeptides comprising SEQ ID NO:9 and biologically active fragments thereof." Furthermore, as described above, the terms "biologically active fragments" or "bioactive fragments" of

SAMP32 encompass natural or synthetic portions of those polypeptides that are capable of specific binding to at least one of the natural ligands of the native polypeptide (see specification, page 6, lines 1-4).

The arguments presented above for claim 10 asserting that it complies with the written description requirement apply with equal force here to claim 18, particularly with respect to the fact that both claims 10 and 18 have been amended. Applicants respectfully submit that this amendment is amply supported in the specification as filed and by that which was known to those of skill in the art at the time the application was filed.

The Examiner has rejected claim 30, asserting that a "fragment" of SEQ ID NO:9 could be an active lysine. Although not necessarily agreeing with the reasoning of the Examiner, Applicants have amended claim 30 by adding the term "bioactive", thus, the claim now recites "bioactive fragment". This amendment is fully supported by the specification as filed. As discussed above for amended claims 10 and 18, and new claim 32, claim 30 as amended is adequately described in the specification as filed. That is the composition for inducing for inducing an immune response now recites a polypeptide comprising SEQ ID NO:9 or a bioactive fragment of SEQ ID NO:9. Furthermore, peptide is defined as 3 or more amino acids at page 4, lines 3-6 of the specification as filed- thus it could not be lysine. Such fragments would be appreciated by those of ordinary skill in the art and are acceptable under *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996), Ex parte Bandman, No. 2004-2319 (BPAI 2005), and Utter v. Hiraga, 845 F.2d 993, 998, 6 USPQ2 1709, 1714, Fed. Cir. 1988.

Applicants respectfully submit that this amendment is amply supported in the specification as filed and by that which was known to those of ordinary skill in the art at the time the application was filed.

Applicants assert that claims 10, 18, and 30 as amended, as well as new claim 32, are in condition for allowance and are adequately described in the specification as filed. Therefore, the rejection as to claims 10, 18, and 30 is now moot and Applicants request that this rejection be withdrawn.

Response to 35 U.S.C. § 103(a), obviousness rejection

Examiner asserts that claim 18 is unpatentable over Kokolus et al. (U.S. 5,807,978). Applicants respectfully that claim 18 as amended is not obvious over Kokolus.

Preliminarily, the three-prong test which must be met for a reference or a combination of references to establish a *prima facie* case of obviousness has not been satisfied in the instant matter. The MPEP states, in relevant part:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. MPEP § 2142.

Additionally, MPEP § 2143.01 provides: "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)."

None of these criteria have been met here.

Claim 18 as amended now recites:

"An antigenic composition comprising a ~~SAMP32~~ bioactive polypeptide of claim 10, and a pharmaceutically acceptable carrier".

Kokolus merely discusses prostate specific antigens. Nowhere does Kokolus disclose or even contemplate novel testis and sperm-specific proteins such as those comprising novel SEQ ID NO:9, as disclosed in the present application (see specification, page 6, lines 15-20; page 22, lines 8-24; Fig. 2; and Example 2, at page 30). Nor does Kokolus contemplate or suggest use of such an antigenic peptide for contraceptive use as disclosed in the present application (see specification, page 6, lines 18 and 19; page 10, lines 30-31).

First, there is no teaching or suggestion in Kokolus to modify Kokolus and arrive at the present invention. One of ordinary skill in the art would not be motivated modify a prostate specific protein and arrive at a testis-specific peptide related to SEQ ID NO:9 as

recited in amended claim 18. Second, there could be no reasonable expectation of success. If the peptides of Kokolus were used as antigens, such prostate specific peptides have dissimilar sequences to SEQ ID NO:9. Therefore, they could not be used as antigenic compositions comprising a peptide of claim 10, as recited in amended claim 18, which could be useful as a contraceptive or in rendering an immune response against such a sequence. Kokolus' mere use of prostate peptides as antigens cannot render obvious the use of the peptides of claim 10 as antigens in claim 18. Third, Kokolus does not teach all of the claimed elements. Kokolus does not teach any of the elements of dependent claim 18, much less independent claim 10, from which claim 18 depends. Therefore, Kokolus cannot render dependent claim 18 obvious.

Applicants respectfully submit that claim 18 as amended is not obvious over Kokolus and request that the obviousness rejection as to claim 18 be withdrawn.

Response to Objections

Claims 11 and 31 were objected to because they depended from rejected independent claims. Applicants submit that the objection has been overcome because the independent claims have been amended and are in condition for allowance. Therefore, Applicants respectfully request that the objections as to claims 11 and 31 be withdrawn.

Conclusion-

The claims, as amended, are believed to be in condition for allowance and applicants hereby request the withdrawal of the rejection under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 103.

Therefore, Applicants respectfully request the issuance of the Notice of Allowance and Issue Fee Due as to claims 10, 11, 18, 30 31, and new claim 32.

Respectfully submitted,

Rodney L. Sparks
Registration No. 53,625
University of Virginia Patent Foundation
1224 West Main Street, Suite 1-110
Charlottesville, VA 22903
(434) 243-6103